REMARKS

Reconsideration and withdrawal of any rejections of the application, and allowance of the claims, especially in view of the remarks made herein, are respectfully requested.

I. STATUS OF THE CLAIMS

Claims 47-72 are pending in the application. Claims 48, 52-54 and 63 have been amended, and new claims 66-72 added, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel.

No new matter is added.

It is respectfully submitted that the claims herewith and the claims as originally presented are and were in full compliance with the requirements of 35 U.S.C. §§101, 102, 103 and 112. The amendments and additions to these claims, and remarks concerning these claims, were not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather for clarification and to round out the scope of protection to which the Applicant is entitled.

Support for the both the amended recitations and the new claims is found throughout the specification and from the originally filed claims.

Specifically, support for amended claim 48 may be found on page 11, lines 10 to 14.

Support for amended claim 52, and new claims 66-72, may be found at page on page 28, lines 3-5 and page 35, lines 22 to 30.

II. THE SECTION 112, NEW MATTER REJECTIONS ARE OVERCOME

Claims 47-65 are rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor was in possession of the invention at the time of filing. The rejection is respectfully traversed.

The Office Action states that "Applicant is claiming new matter in claim 47 by reciting a method of increasing the relative number of CD45 low cells." It is respectfully submitted that this recitation is not new matter.

The claims are directed to a method of "increasing the relative number of CD45 low cells in a cell population, wherein the population includes committed hemopoietic cells comprising

CD45 antigen, which method comprises: (i) contacting the cell population with an agent that operably engages said committed cells; and (ii) incubating committed cells that are engaged by said agent such that the relative number of CD45 low cells increases as a result of said engaging."

The Examiner notes that page 28 of the specification teaches that "treatment of peripheral blood samples with antibody to the HLA-DR beta chain increases the relative number of CD45 low cells." The Office Action continues to state that the specification fails to point out that the CD45 low population would be of any particular interest for one to prepare, and that "since one would not have been led to consider this particular cell population, applicant was not in possession of the invention at the time of filing." The Applicant respectfully disagrees with this assessment.

The CD45 low cell population is described in the specification on page 28, as mentioned in the Office Action. However, the results of the experiment described on pages 28-29 are also contained within Table 6 and Charts 1-5. Additionally, the CD45 low populations are again discussed on page 34 and in Table 8.

The Examiner is respectfully reminded that the specification must be read in the context of the state of the art at the time of filing. It is respectfully submitted that, at the time of filing, an individual of skill in the art would have been readily aware of the usefulness of undifferentiated cells possessing CD45 low markers. This very sentiment is presented by the Applicant in the accompanying Declaration of Dr. Illham M.S.S. Abuljadayel under 37 C.F.R. §1.132. It is respectfully submitted that Dr. Abuljadayel is an expert in the field of immunology. In demonstration of this, attached is a partial list of articles authored or co-authored by Dr. Abuljadayel.

The Examiner's attention is respectfully drawn to section 5 of the attached declaration, entitled "Utility." The text of the section is set forth below:

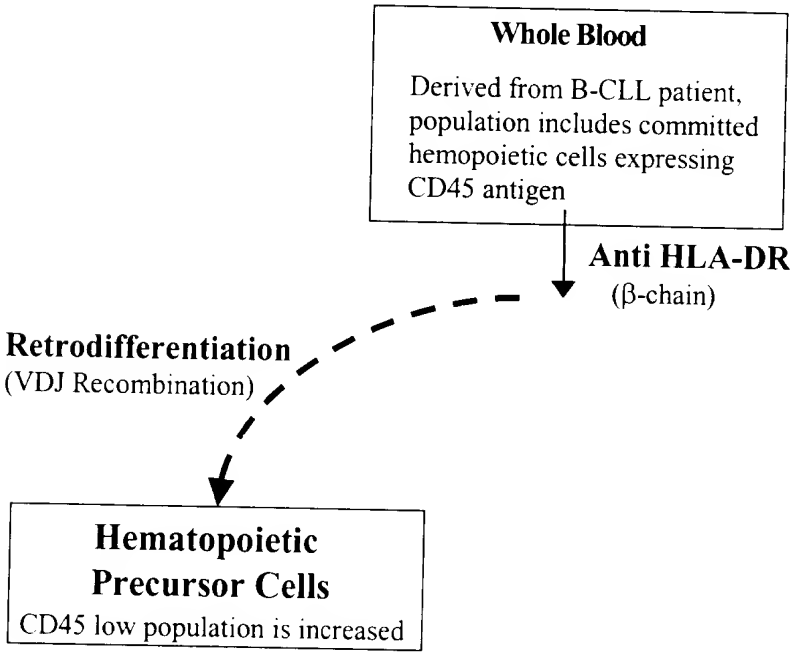
> As would have been readily understood at the priority date of the present invention, i.e. at February 2, 1995, CD45low is a marker found on stem cells having a haemopoietic or myeloid nature. A skilled person at the priority date of the above-identified application would have readily understood that undifferentiated cells with CD45low markers could be used in the production of, *inter alia*, more committed haematopoietic cells, for example white blood cells. Thus, CD45low cells could be redifferentiated into more committed haematopoietic cells for instance, and thus a

skilled person would have readily understood that the CD45low cells had a utility in the treatment of, for example, leukaemia.

Thus, one of skill in the art would recognize the value of being able to, *inter alia*, increase the relative number of CD45 low cells in a cell population. Furthermore, the teaching in the specification, as found on pages 28-29 and 34, would provide one of skill in the art with the methods of accomplishing the same. Specifically, the Examiner's attention is drawn to the following experiment, as described in the specification, which demonstrates the method of increasing the relative number of CD45 low cells in a population:

> All human leukocytes are $CD45^{+}$. Undifferentiated cells are CD45 low. Treatment of blood samples with monoclonal antibody to the homologous region of the chain of the HLA-DR antigen increased the relative number of CD45 low cells, which coincided with a decrease in the relative umber of CD45 high cells, indicating that B cells were retrodifferentiating into undifferentiated cells. *See* the Specification, page 28. The appearance of the undifferentiated cells occurred over time. *See* the Specification, page 29 (Table 6 shows the results of patient numbers 2, 3 and 4 which represent samples analyzed from the same patient over time).

Blood Sample +	Anti HLA - DR	=	Undifferentiated Cells
Mixed Population	mAb to β-chain		**CD45 low**



Thus, one of skill in the art, at the time of filing, would have recognized the potential usefulness of being able to increase the relative number of CD45 low cells in a given cell population. Additionally, as set forth above, the method of increasing the relative number of CD45 low cells is explicitly set forth in the specification. Consequently, the recitation of "increasing the relative number of CD45 low cells" in the claims is **not** new matter. Rather, the disclosure of such a method was present in the specification at the time of filing, and the usefulness of such a method was known to one of skill in the art. Clearly, the Applicant was in possession of the invention at the time of filing, as evidenced by the detailed example set forth on pages 28 to 29 of the specification, which is significantly more substantial than the "not[ing] [of] this increase as an interesting observation pertaining to the expression of a particular antigen present on all human leukocytes." Consequently, the section 112, new matter rejection, cannot stand. Consequently, reconsideration and withdrawal of the rejection is respectfully requested.

Claim 48 has also been rejected as allegedly containing new matter. Specifically, the Office Action objects to the recitation where the agent "engages a receptor that mediates capture recognition or presentation of an antigen at the surface." The rejection is respectfully traversed.

It is respectfully submitted that Claim 48 has been amended herewith, rendering the rejection moot. Consequently, reconsideration and withdrawal of the rejection is respectfully requested.

Additionally, claim 49 has been rejected as allegedly containing new matter. Specifically, the Office Action states that the recitation "2 to 24 hours" is new matter. The rejection is respectfully traversed.

The Examiner's attention is respectfully drawn to Table 6 of the current application. The left hand column of the Table lists the times for which cell populations were incubated. It is noted that the incubation times are within 2 to 24 hours, which data provides the basis for the recitation in question.

As the recitation "2 to 24 hours" is clearly described in Table 6, it is respectfully suggested that the rejection cannot stand. Consequently, reconsideration and withdrawal of the rejection is respectfully requested.

Claim 52 is also rejected as allegedly containing new matter. Specifically, the Examiner states that there is no support in the disclosure for claiming that "CD45+ committed cells include the variously recited colony forming cells." The rejection is respectfully traversed.

Claim 52 has been amended herewith, rendering the rejection moot. Specifically, as pointed out above, support for amended claim 52 is found at page 28, lines 3 to 5, and at page 35, lines 22 to 30. Kindly note that page 35, lines 22 to 30 discuss the CD34 antigen. It is respectfully submitted that one of skill in the art would recognize that CD34+ cells are always CD45 low, such that details concerning CD34+ cells may also be applied to CD45 low cells. Consequently, reconsideration and withdrawal of the rejection is respectfully requested.

Claim 53 is also rejected as allegedly containing new matter. Specifically, the Office Action states that there is no teaching at pages 28-29 that the "detected population of CD45 low cells is MHC class I+ or class II+." The rejection is respectfully traversed.

The Examiner's attention is respectfully drawn to page 2, lines 29 to 31, wherein the specification states that "[m]ost undifferentiated and differentiated cells comprises Major Histocompatability Complex (MHC) Class I antigens and/or Class II antigens...[i]f these antigens are associated with those cells then they are called Class I+ or Class II+ cells." Additionally, at page 9, the specification reads "[p]referably, the undifferentiated cell is an MHC Class I+ and/or an MHC Class II+ cell...preferably, the undifferentiated cell is a CD34+ cell." As we have already distinguished that all CD34+ cells are CD45 low, any statements in the specification relating to CD34+ may be extrapolated to CD45 low cells. Consequently, page 9 of the specification provides support for the recitation of claim 53.

Reconsideration and withdrawal of the rejection is respectfully requested.

III. THE SECTION 112 REJECTIONS ARE OVERCOME

Claims 47-65 were rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey that the inventor had possession of the invention at the time of filing. The rejection is respectfully traversed.

Specifically, the Office Action states that the Applicant was not in possession of the genus of agents which operably engage committed cells (specifically directed towards claims 47-61 and 63-65), nor of the genus of "biological response modifiers."

The Examiner's attention is respectfully drawn to the accompanying Declaration, in which further examples are set forth which utilize a variety of agents which engage committed cells.

Specifically, the Examiner's attention is drawn to section 4.5 (Conclusion) of the Declaration, which states in part:

> ...the agents,
> (i) monoclonal antibody to the homologous region of the beta chain of the HLA-DR antigen;
> (ii) monoclonal antibody to the homologous region of the beta chain of the HLA-DR antigent with cyclophosphamide;
> (iii) monoclonal antibody ot the homologous region of the class I antigens;
> (iv) GM-CSF
> (v) erythropoietin;
> (vi) monoclonal antibody to the alpha chain of MHC class II antigen (TAL.IB5);
> (vii) anti-C2 and anti-CD33 antibodies secondarily labeled with anti-mouse coated magnetic beads;
> (viii) and monoclonal antibody to the beta chain of MHC class II antigen (CR3/43);
> resulted in an increased number of cells with the marker CD45low when the cell population was contacted with the agent and the cells engaging the agent were incubated.

The additional data provided in the Declaration demonstrates that agents other than antibodies directed towards the alpha or beta chains of MHC Class I or II may be used to generate an increasing number of cells with the CD45 low marker. Accordingly it is submitted that Applicants were in possession of the agents which operably engage committed cells.

Furthermore, the Office Action also states that Applicants were not in possession of the genus of "biological response modifiers" at the time of filing. The Office Action also states that the only biological response modifier which is exemplified in the specification is cyclophosphamide.

The Examiner's attention is drawn to Example 4 of the accompanying Declaration, in which cortisol is used as a biological response modifier. As cortisol is a hormone, it falls squarely within the grouping described on page 14, lines 4-6 of the specification, and is therefore representative of the genus. These biological response modifiers are used in conjunction with the agents of the present invention, and are necessary for obtaining certain specific populations of cells. For instance, to obtain haematopoietic cells, cortisol in Dexter medium is used, whereas to obtain neuronal stem cells, mercaptoethanol in embryonic stem cell medium is used.

All of the foregoing illustrate that the Applicant was clearly in possession of the genus of biological response modifiers at the time of filing. Consequently, reconsideration and withdrawal of the section 112 rejections is respectfully requested.

The Office Action has also raised new section 112 rejections which are now presented.

Claims 54-65 were rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is respectfully traversed.

Claims 54 and 63 have been amended herewith, rendering the rejection moot. Consequently, reconsideration and withdrawal of the rejection is respectfully requested.

IV. THE SECTION 101 REJECTIONS ARE OVERCOME

Claims 47 to 65 are rejected under 35 U.S.C. §101 because the claimed invention is allegedly not supported by either a specific asserted utility or a well established utility. Claims 47 to 65 are also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is allegedly not supported by either a specific asserted utility or a well established utility, one of skill in the art would not know how to use the claimed invention. The rejections are respectfully traversed.

Specifically, the Examiner's attention is again directed to section 5 of the accompanying declaration, in which the Applicant describes the utility of the invention, and states that one of skill in the art, at the time of filing, would have known of the potential uses for a population of cells in which the relative number of CD45 low cells is increased. As evidenced in the accompanying Declaration, one such use would be in the treatment of leukemia.

In light of the accompanying Declaration and the remarks herein, reconsideration and withdrawal of the rejections are respectfully requested.

V. THE DOUBLE PATENTING REJECTION IS OVERCOME

Claims 47-66 and 68-87 were rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 1-20 of U.S. Patent No. 6,090,625. The rejection is respectfully traversed.

The Office Action states that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other." Applicants respectfully disagree.

However, while Applicants do not agree that there is double patenting between the current application and U.S. Patent No. 6,090,625, in an effort to further prosecution of the present application, Applicants will file a terminal disclaimer upon notification of allowable subject matter. Until such time, it is respectfully requested that the rejection be held in abeyance.

Consequently, reconsideration and withdrawal of the double patenting rejection is respectfully requested.

REQUEST FOR INTERVIEW

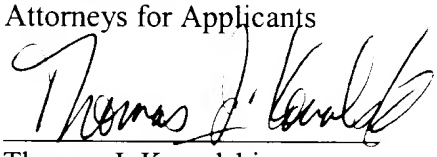
If any issue remains as an impediment to allowance, prior to any paper issuing other than a Notice of Allowance, another interview is respectfully requested and the Examiner is further respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for the interview.

CONCLUSION

In light of the amendments and remarks made herein, it is respectfully submitted that the application is now in condition for allowance. Early and favorable reconsideration of the application, reconsideration and withdrawal of the rejections of the application, and prompt issuance of a Notice of Allowance are earnestly solicited.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for Applicants

By: 

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

48. (Amended) The method according to [of] claim 47, wherein the agent engages a receptor [that mediates capture, recognition or presentation of an antigen at the surface of the committed cells] by direct engagement or indirect engagement.

52. (Amended) The method according to claim 47, wherein the committed cells are [selected from T-cell colony-forming cells (CFC-T cells), B-cell colony-forming cells (CFC-B cells), eosinophil colony-forming cells (CFC-Eosin cells), basophil colony-forming cells (CFC-Bas cells), granulocyte/monocyte colony-forming cells (CFC-GM cells), megakaryocyte colony-forming cells (CFC-MEG cells), erythrocyte burst-forming cells (BFC-E cells), erythrocyte colony-forming cells (CFC-E cells), T cells and B cells] human leukocytes, wherein the human leukocytes are found in peripheral blood, bone marrow, thymus, spleen or tonsil tissue, and wherein the leukocytes are selected from the group consisting of lymphocytes, monocytes, polymorphonuclear cells, eosinophils and basophills.

53. (Twice Amended) The method according to claim 48[47] wherein the CD45 low cells are Major Histocompatibility Complex (MHC) class I^+ and/or MHC class II^+ cells.

54. (Amended) The method according to claim 47 [53], wherein the receptor is an MHC class I antigen or an MHC class II antigen.

63. (Amended) A method according to claim 47 wherein the agent is used in conjunction with a biological response modifier as defined herein.

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PMID: 1550409 [PubMed - indexed for MEDLINE]

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Klebsiella antibodies in ankylosing spondylitis and Proteus antibodies in rheumatoid arthritis.

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